High-Resolution Manometry in Clinical Practice

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Abstract: High-resolution manometry (HRM) is the primary method used to evaluate esophageal motor function. Displayed and interpreted by esophageal pressure topography (EPT), HRM/EPT provides a detailed assessment of esophageal function that is useful in the evaluation of patients with nonobstructive dysphagia and before foregut surgery. Esophageal motility diagnoses are determined systematically by applying objective metrics of esophageal sphincter and peristaltic function to the Chicago Classification of esophageal motility disorders. This article discusses HRM study, EPT interpretation, and the translation of EPT findings into clinical practice. Examples are provided to illustrate several clinical challenges.

Esophageal manometry is recommended for the evaluation of patients with nonobstructive dysphagia and before antireflux surgery.1 Manometry is also sometimes used for the assessment of noncardiac chest pain and the evaluation of patients with other symptoms, such as regurgitation, especially if there is clinical concern for achalasia. In high-resolution manometry (HRM), catheters with pressure sensors spaced 1 to 2 cm apart are positioned to span a length extending from the hypopharynx to the stomach so that pressures generated along the entire length of the esophagus can be measured simultaneously. Sophisticated software processes the HRM pressure output by using interpolation to generate esophageal pressure topography (EPT) plots that represent esophageal motility and sphincter function on color-coded, pressure-space-time plots.2 Analysis of the EPT plots is facilitated by objective metrics of esophageal function that are generated by the analysis software and can be applied to classify individual swallows and generate an esophageal motility diagnosis. A classification scheme was initially proposed based on the analysis of clinical studies performed at Northwestern University and subsequently named the Chicago Classification of esophageal motility disorders.3,4 Since its development, the Chicago Classification has been periodically updated by an international working group to incorporate ongoing clinical and research experience.5,7

The enhanced pressure resolution and objective metrics available with HRM/EPT are thought to provide a more accurate and...
reliable diagnosis of esophageal motility disorders than conventional manometry, which uses pressure sensors spaced 3 to 5 cm apart and is analyzed as line tracings. Since its introduction into research and clinical practice approximately a decade ago, HRM/EPT has made possible the identification of distinct clinical phenotypes of esophageal motor disorders. The aim of this article is to discuss the use and interpretation of HRM/EPT and how, as illustrated by examples, HRM/EPT findings can be translated into clinical practice.

High-Resolution Manometry Study

After catheter calibration and the application of a topical anesthetic to the patient’s naris and/or throat, the HRM catheter is placed transnasally and positioned with the pressure sensors spanning a length extending from the hypopharynx, through the esophagus, to 3 to 5 cm within the stomach. After a brief period to allow patient acclimation, a baseline of resting pressures can be obtained during approximately 30 seconds of easy breathing without swallows. Correct catheter placement to traverse the esophagogastric junction (EGJ) can be confirmed during this period by recognition of the presence of the pressure inversion point (PIP), which is the point at which the inspiration-associated negative intrathoracic pressure inverts to the positive intra-abdominal pressure. Having the patient take deep breaths facilitates identification of the PIP by augmenting the EGJ pressure and exaggerating the intrathoracic and intra-abdominal pressures.

The Chicago Classification is based on the analysis of 10 supine liquid swallows (5 mL of water). Other components can be added to the manometric protocol to supplement clinical interpretation. The inclusion of upright swallows can be useful to help determine if abnormal pressure signals, particularly at the EGJ, are related to anatomic abnormalities, such as vascular artifact or hiatal hernia. Incorporating swallows of boluses with different textures (thick liquids or solids) or a test meal may also be beneficial to uncover symptoms and/or abnormal findings of esophageal function. However, it should be noted that changing position (supine vs upright) and bolus consistency results in an alteration in generated pressures, such as reduced lower esophageal sphincter (LES) relaxation pressures with upright rather than supine swallows; consequently, swallows must be interpreted accordingly. Multiple rapid swallows (generally 5 swallows of 2 mL of water spaced at 2- to 3-second intervals) can also be included to elucidate defects in deglutitive inhibition (if esophageal contractions occur during the course of the multiple swallows) and to assess for peristaltic reserve. Peristaltic reserve can be identified by augmentation of the esophageal contractile vigor following the multiple swallows and may help to predict risk for the development of postfundoplication dysphagia or to detect a cause of symptoms in a patient with an otherwise normal manometry study.

At our institution, the standard protocol includes the following: 10 supine liquid swallows; 5 upright liquid swallows (5 mL of water); multiple rapid swallows (5 swallows of 2 mL of water spaced at 2- to 3-second intervals); and provocative swallows with a thick liquid (applesauce) bolus and a solid food (crackers) bolus.

Interpretation of Esophageal Pressure Topography

EPT studies can be interpreted in a stepwise, hierarchical fashion directed by the Chicago Classification. However, several caveats should be noted when the Chicago Classification is applied to EPT analysis. First, the absolute values reported in the Chicago Classification (and in the remainder of this article) are based on normative values generated with the Sierra HRM assembly (Given Imaging) from supine swallows of 5 mL of water. Thus, the interpretation of manometry studies performed using different catheter assemblies, patient positions, and/or boluses (volume and/or consistency) requires the recognition of expected differences in the normative values of EPT metrics, which have been summarized in a review by Herregods and colleagues. Additionally, the Chicago Classification is based on the assessment of patients without previous foregut surgery; therefore, technically it should not be applied in patients with previous foregut surgery. However, with acknowledgment of these factors, the concepts of EPT interpretation based on the Chicago Classification can be broadly applied.

Basal Esophagogastric Junction and Upper Esophageal Sphincter Assessment

Although not incorporated in the Chicago Classification of esophageal motility diagnoses, EGJ morphology and basal pressure, as well as upper esophageal sphincter (UES) characteristics, are often assessed with HRM/EPT. The basal EGJ pressure should be assessed during a period of quiet breathing without swallows. Because the crural diaphragm contributes to EGJ pressure, both the separation of the LES and crural diaphragm (ie, EGJ morphology) and the effect of the respiratory cycle on the basal EGJ pressure should be appreciated; greater separation of the LES and crural diaphragm and reduced crural diaphragm augmentation pressures are associated with increased reflux. Elevated basal EGJ pressures are also observed, but the clinical relevance of this finding remains unclear. Thus, although we report EGJ morphology and basal pressures in our own practice, the application of these findings in our clinical management is fairly minimal.
Because HRM catheters allow pressure sensors to be placed at 1-cm intervals throughout the hypopharynx and proximal esophagus, HRM/EPT carries the potential for UES evaluation, although reports to date of this clinical use are limited. Exaggerated respiration-associated changes in UES pressure and elevated postswallow residual pressures have been reported in patients with globus.\textsuperscript{17,18} Furthermore, the incorporation of combined intraluminal impedance and manometry may be useful to evaluate pharyngeal bolus flow and swallowing function.\textsuperscript{19,20}

**The Chicago Classification: Individual Swallow Assessment**

The initial step in applying the Chicago Classification to determine an esophageal motility diagnosis is to classify individual swallows by applying EPT metrics of deglutitive LES relaxation and esophageal body contractility and/or peristalsis (Figures 1 and 2).\textsuperscript{7}

**Deglutitive Lower Esophageal Sphincter Relaxation**

Deglutitive LES relaxation is measured with HRM/EPT by using the integrated relaxation pressure (IRP; Figure 1). Because the IRP is referenced to gastric pressure, it can be affected by abnormal pressurization within the stomach. Therefore, we typically place the gastric reference 2 cm below the EGJ, although we may adjust the placement of the gastric reference to reflect the esophageal outflow resistance pressure. This typically applies in the setting of hiatal hernia, in which the reference is placed within the hernia and/or below the crural diaphragm to represent the optimal esophageal outflow resistance.

**Distal Latency**

The contractile deceleration point (CDP) has been recognized as an important landmark that represents the physiologic transition from esophageal peristalsis to ampullary formation and emptying.\textsuperscript{21} Clinically, the primary importance of identifying this landmark is in defining the distal latency (Figure 1), the essential metric for spastic contractions.\textsuperscript{22,23} Although some studies of patients appear to contain multiple deceleration points along the contractile wave front, the CDP should represent the transition to the terminal propagating velocity and should be within 3 cm of the EGJ.\textsuperscript{7,21}

**Peristaltic Vigor**

Peristaltic vigor is measured in HRM/EPT by the distal contractile integral (DCI; Figure 1). Because one of the goals of the most recent update of the Chicago Classification was to simplify the esophageal motility assessment with EPT, the DCI was given greater importance in the schema for individual swallow assessment.\textsuperscript{7} The DCI was used solely as the metric to define esophageal body hypercontractility in previous versions of the Chicago Classification; however, the DCI is also used in the most recent version as a measure of hypocontractility.\textsuperscript{3,6,7,24} Hypercontractile swallows are defined by a DCI higher than 8000 mmHg$\times$s$\times$cm, a value previously exceeding any observed DCI in studies of normal controls. Swallows with a DCI lower than 450 mmHg$\times$s$\times$cm showed strong agreement with ineffective swallows identified on conventional manometry, and so a lower DCI threshold has been incorporated into the classification scheme to define ineffective swallows.\textsuperscript{7,25}

**Peristaltic Integrity**

In swallows with a normal DCI, the integrity of the peristaltic wave is assessed by measuring the length of
Axial breaks in the 20-mmHg isobaric contour. Previous versions of the Chicago Classification labeled breaks as small (3-5 cm) or large (>5 cm), although the most recent update classifies only swallows with large peristaltic breaks (ie, >5 cm) as fragmented swallows (Figure 3).

Pressurization Pattern

The final step in assessing individual swallows is to determine the pressurization pattern. With the isobaric contour set at 30 mmHg, swallows are assessed for panesophageal pressurization (ie, esophageal pressurization simultaneously extending from the UES to the EGJ) and/or compartmentalized pressurization (ie, distal esophageal pressurization extending from the contractile front to the EGJ).

The Chicago Classification: Esophageal Motility Diagnosis

After the analysis of 10 supine water swallows, the composite deglutitive LES relaxation measurements (the median IRP) and designations of swallow type can be applied systematically to the Chicago Classification to provide an esophageal motility diagnosis (Figure 4).7

Abnormal Deglutitive Lower Esophageal Sphincter Relaxation

Perhaps the most important measurement obtained with esophageal manometry is that of deglutitive LES relaxation, which is the initial decision point in the Chicago Classification algorithm. Abnormal deglutitive LES relaxation is the hallmark of achalasia, which is the best-described esophageal motility disorder, and the one for which the most effective and standardized treatments are available.26

In addition to elevated deglutitive LES relaxation pressures, achalasia can be further subclassified according to the esophageal body pressurization pattern.27 Type I (classic) achalasia is identified by 100% failed swallows, type II achalasia by panesophageal pressurization, and type III (spastic) achalasia by premature (or spastic) swallows.
The differentiation of achalasia into subtypes provides prognostic information that helps to predict response to treatment (i.e., pneumatic dilation or Heller myotomy).27-31 Type II achalasia, the most common subtype, is the one most likely to have a positive treatment outcome (response rates of 85%-95%), followed by type I achalasia (response rates of 56%-85%).27-31 Type III achalasia is the least common subtype and has the poorest response rates, ranging from 29% to 69%. The randomized, prospective European Achalasia Trial, which compared pneumatic dilation and Heller myotomy, demonstrated similar outcomes for the therapies among all patients with achalasia; however, the follow-up analysis evaluating outcome according to achalasia subtype suggested that patients with type III achalasia may derive greater benefit from Heller myotomy.30,32 Additionally, the anatomic location and/or extent of spastic esophageal contractions can be identified with EPT, which may facilitate the determination of the required myotomy length. However, the use of tailored myotomy, which possibly can be facilitated with peroral esophageal myotomy (POEM), to treat type III achalasia has not been systematically studied.

Elevated deglutitive LES relaxation pressure is defined in the most recent Chicago Classification as an elevated median IRP higher than 15 mmHg; however, varying IRP thresholds depending on the achalasia subtype have been proposed.33 Using a classification and regression tree model and IRP cutoffs of 10 and 17 mmHg for type I and type III achalasia, respectively, and defining type II achalasia by the presence of panesophageal pressurization regardless of the IRP, improved the sensitivity of the diagnosis of achalasia in comparison with the traditional,
algorithm-based Chicago Classification.34 Thus, in the case of a patient who has borderline deglutitive LES relaxation pressures with absent esophageal contractility or panesophageal pressurization (Figure 5), a diagnosis of achalasia may remain in consideration.

When abnormal deglutitive LES relaxation is present in addition to an esophageal body contractility pattern that does not meet the criteria for an achalasia subtype (eg, with residual peristaltic activity), a diagnosis of EGJ outflow obstruction is reached. This disorder is so named because of a manometric pressure pattern similar to that of patients with postfundoplication dysphagia and may represent mechanical obstruction, such as hiatal hernia, extraesophageal obstruction, infiltrating disease of the esophageal wall, or early achalasia.35 In a retrospective study of 57 patients with esophageal motility disorders who underwent endoscopic ultrasound (EUS) evaluation, 9 patients (16%; 5 with EGJ outflow obstruction and 4 with type I or II achalasia) had a clinically significant lesion identified on EUS.36 Thus, we often pursue EUS or other imaging before offering invasive intervention directed at relieving the EGJ outflow obstruction, such as Heller myotomy.35

**Major Disorders of Peristalsis**

Absent contractility, distal esophageal spasm (DES), and hypercontractile esophagus are considered the major disorders of peristalsis, as these manometric patterns are not observed in normal controls. These disorders typically have normal deglutitive LES relaxation pressures; however, hypercontractile esophagus can occur concomitantly with EGJ outflow obstruction, and, as previously discussed, a diagnosis of achalasia may be considered in a patient with borderline IRP and absent contractility.

Absent contractility is the pattern typically associated with esophageal disease of systemic sclerosis (and so was...
previously referred to as scleroderma esophagus); however, this manometric pattern can be seen in other connective tissue and systemic diseases, including diabetes, myxedema, and multiple sclerosis, among others, or in the absence of systemic disease. The impaired esophageal bolus and acid clearance associated with absent contractility can predispose patients to both gastroesophageal reflux and dysphagia. Promotility agents are typically clinically ineffective; therefore, the treatment of absent peristalsis tends to be directed at reflux disease and incorporates lifestyle modifications and acid suppression.

Premature swallows (ie, swallows with reduced distal latency, defined as <4.5 seconds) are the hallmark of DES. Simultaneous contractions were the traditional defining feature of DES, and DES was initially defined within the Chicago Classification by rapid swallows (ie, swallows with an above-normal contractile front velocity [CFV]). However, based on descriptions of abnormal distal contractile latency representing impaired deglutitive inhibition in patients with simultaneous contractions, subsequent study with HRM/EPT helped redefine DES into a more clinically specific entity. Patients with abnormal distal latency, although rare, uniformly presented with a predominant symptom of dysphagia and/or chest pain. However, the group of patients who had a rapid CFV (>9 cm/s) without abnormal distal latency was heterogeneous, primarily consisting of patients with weak or otherwise normal peristalsis. Thus, classifying swallows based on CFV measurement is of questionable clinical significance, and use of the CFV for the classification of esophageal motility disorders has been omitted from the recent Chicago Classification update. However, although the use of distal latency appears to identify a specific clinical entity, clinical outcome studies comparing the diagnostic use of distal latency, CFV, and/or other markers of simultaneous contractions are still needed.

Hypercontractile esophagus is defined as 2 or more hypercontractile swallows. This disorder is sometimes referred to as jackhammer esophagus because of the frequency of respiration-independent multiple-peaked contractions. A study describing a patient population with hypercontractile swallows identified a unique clinical phenotype with a manometric pattern not observed in normal controls. Although the patients who had hypercontractile swallows manifested primarily with dysphagia, clinical heterogeneity was observed within this patient population, with some patients demonstrating EGJ outflow obstruction or reflux disease. The mechanism of hypercontractile esophagus is unknown, although there have been several proposed hypotheses, such as the response to mechanical obstruction, defects of innervation affecting deglutitive inhibition, and/or abnormalities of longitudinal muscle function. Hypertensive peristalsis, or nutcracker esophagus, defined by a mean DCI of 5000 to 8000 mmHg cm (a value higher than that of the 95th percentile of normal controls), was previously described in the Chicago Classification. However, the clinical significance of this finding has been questioned, and so this diagnosis has been omitted from the most recent version of the Chicago Classification.

The management of DES and hypercontractile esophagus can be challenging. A conundrum is that although symptoms of dysphagia and chest pain are common in patients who demonstrate reduced latency or hypercontractile swallows on stationary manometry, symptoms typically do not occur during the manometry study; thus, symptoms often carry a poor temporal association with abnormal manometry findings (Figure 6).
Although ambulatory manometry studies with conventional assemblies have demonstrated some symptom association with prolonged, high-amplitude esophageal contractions, similar studies have not been reported with HRM. Thus, it is not surprising that medical treatments targeting abnormal manometry parameters, such as calcium channel blockers, nitrates, and phosphodiesterase inhibitors, have demonstrated mixed results in clinical studies. Some success has been reported with botulinum toxin A (Botox, Allergan) injections and POEM. However, it should be noted that to date, clinical studies of DES and nutcracker esophagus have typically had small sample sizes and patients with varying conventional manometry–defined inclusion criteria. Thus, further study based on HRM/EPT-identified patient populations with specific, clinically relevant phenotypes of DES and hypercontractile esophagus is needed.

**Minor Disorders of Peristalsis**

Because there is some overlap with manometric patterns observed in normal controls, ineffective esophageal motility (IEM) and fragmented peristalsis are considered minor disorders of peristalsis. However, these motility diagnoses are commonly encountered when patients with both dysphagia and reflux symptoms are evaluated. Although both IEM and large peristaltic defects (ie, fragmented peristalsis) are associated with abnormal bolus transit and dysphagia, their clinical significance and the subsequent direction of therapy based on the manometric findings remain unclear. Thus, treatment typically involves the control of acid reflux with modification of diet and lifestyle and adjustment of medications and dosing to facilitate esophageal transit (Figure 3), such as the use of liquid formulations, maintaining an upright position after pill ingestion, and the avoidance of unnecessary medication and/or supplements. Additionally, a diagnosis of functional dysphagia or heartburn and a trial of neuromodulator therapy are often considered, although the evidence to support this approach is limited.

**Incorporation of High-Resolution Impedance Manometry**

The incorporation of multiple impedance sensors, which detect the presence of air or liquid by measuring changes in electrical resistance, on HRM catheters allows the simultaneous measurement of bolus transit and bolus clearance as they relate to esophageal pressures. In patients with achalasia, measurement of the impedance bolus height after 200 mL of dilute saline had been swallowed correlated with measurement of the barium column height on timed barium esophagram in the assessment of bolus retention. The primary function of the esophagus
Figure 7. A patient with rumination syndrome. A postprandial high-resolution impedance manometry (HRIM) study was obtained for a 25-year-old woman referred for the evaluation of regurgitation and occasional heartburn with minimal response to proton pump inhibitor therapy. She had a history of bulimia nervosa. Her upper gastrointestinal endoscopy findings were normal, as was distal esophageal acid exposure on a 24-hour pH-impedance test. Although the diagnosis was clinically suspected, the HRIM study helped to confirm it. The rumination events, as depicted here, were identified by increases in abdominal pressure preceding liquid reflux, identified as an impedance decrease of 50% (white line tracings) and purple coloring (interpolated high-resolution impedance output). The patient was referred for cognitive behavioral therapy with biofeedback, and her condition significantly improved.

Figure used with permission from the Esophageal Center at Northwestern University Feinberg School of Medicine.

is to transport and clear bolus, and the use of high-resolution impedance manometry (HRIM) may enhance the evaluation of esophageal function as it pertains to bolus transport. HRIM may also aid the assessment of oropharyngeal swallowing dysfunction. Methods incorporating HRIM to measure the intrabolus pressure relative to peak esophageal peristaltic pressure through the EGJ and/or during phases of esophageal bolus transport have also been reported. Although these methods may aid in the evaluation of esophageal function and symptom generation, further study is needed to demonstrate their role in directing patient treatment decisions.

Evaluation of Refractory Reflux/Regurgitation

Another area of clinical practice in which HRIM may be particularly useful is in the assessment of suspected gastroesophageal reflux disease that does not respond to proton pump inhibitor therapy, especially when the predominant symptom is regurgitation. Esophageal manometry is recommended before antireflux surgery to exclude other potential causes of a patient’s symptoms. Although achalasia is the alternate diagnosis usually considered, HRIM (usually with periods of testing of increased duration) also makes it possible to assess for other clinical diagnoses, particularly rumination syndrome (Figure 7) and supragastric belching, which can typically be identified by air reflux events (abrupt impedance elevations) preceded by UES relaxation in the absence of LES relaxation. Both rumination syndrome and supragastric belching are behavioral disorders that can be clinically diagnosed based on a patient’s history and often with observation of eating behavior; however, HRIM can provide objective evidence of these diagnoses to clinicians and patients and can also be used as a method for biofeedback during initiation of the recommended behavioral therapy (typically diaphragmatic breathing).

Conclusion

HRM and EPT provide a detailed assessment of esophageal function, which has been used to identify clinically distinct phenotypes of esophageal motility. The application of EPT metrics and Chicago Classification concepts facilitates the objective identification of specific motility disorders, although further work to improve the characterization and classification of esophageal motility disorders is ongoing. Although the management of esophageal motility disorders can pose challenges in clinical practice, further systematic study with specific HRM/EPT criteria for inclusion may help translate the gains that have been made in defining the characteristics of esophageal disease into improved treatment outcomes for patients.

This work was supported by T32 DK101363 (J. E. P.) and R01 DK079992 (J. E. P.) from the US Public Health Service.

Dr Carlson has no relevant conflicts of interest to disclose. Dr Pandolfino has received grant support from and has served as a consultant and speaker for Given Imaging. He has also served as a consultant and speaker for Sandhill Scientific, Takeda Pharmaceutical Company, and AstraZeneca.

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